Limited correlation between the Health Assessment Questionnaire (HAQ) and EuroQol in rheumatoid arthritis: questionable validity of deriving quality adjusted life years from HAQ

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Objectives: There is growing emphasis on the cost-effectiveness of treating rheumatoid arthritis. Few trials directly record the health utility measures, like EuroQol, needed for economic analyses. Consequently linear regression methods have been used to transform Health Assessment Questionnaire (HAQ) scores into utility measures. The authors examined whether this is justified.

Methods: The authors compared HAQ and EuroQol in cross-sectional and treatment change observational studies of rheumatoid arthritis patients; they also measured SF-36 and Nottingham Health Profiles.

Results: In the cross-sectional study, HAQ and EuroQol scores were moderately inversely correlated (Spearman rank correlation, $r=0.76$). HAQ showed a Gaussian distribution whereas EuroQol was bimodal. In the treatment change study, changes in HAQ and EuroQol were unrelated ($r=0.08$); the changes showed similar Gaussian and bimodal distributions.

Conclusions: Not all patient-based measures are analogous, and evidence of clinical equivalence, especially in treatment response, is needed before data transformation is considered. Specifically, as HAQ and EuroQol are demonstrably not equivalent, economic evaluations of treatment cost effectiveness should not be based on EuroQol data transformed from HAQ. The use of such transformed data by regulatory bodies which determine drug availability means that the issue is no longer only of academic interest but a real clinical concern.

Patient-based health status measures help assess rheumatoid arthritis in both clinical and research circumstances. They include functional measures such as the Health Assessment Questionnaire (HAQ), quality of life measures such as the Nottingham Health Profile (NHP), quality of life/health status measures such as the SF-36 and indirect utility measures such as the EuroQol.² Their inter-relationships are controversial in rheumatoid arthritis in which quality of life is influenced not only by joint inflammation and function, but also by less specific symptoms such as pain, fatigue and depression.³

Utility measures are preference-based measures of health-related quality of life which summarise positive and negative effects into one value between 0 (equal to death) and 1 (equal to perfect health). They can be transformed into quality adjusted life year (QALY) outcome measures which form the basis of calculating the cost effectiveness of interventions. The advent of high cost treatments such as tumour necrosis factor inhibitors for rheumatoid arthritis has focussed attention on identifying their cost effectiveness.^{4–6} Such studies have produced widely varying estimations of cost per QALY

suggesting that there may be methodological problems. One potential concern is that, because clinical trials in rheumatoid arthritis invariably record HAQ but not necessarily EuroQol or SF-36, health economists have used linear regression equations to mathematically transform changes in HAQ scores into EuroQol^{7,8} data which can be used to calculate QALYs. We believe this approach may be erroneous as it involves mathematical transformation between measures which may not be clinically equivalent. We therefore examined their inter-relationships further.

METHODS

Patients

We studied outpatients with rheumatoid arthritis who met the criteria of the American College of Rheumatology. The study had multicentre research ethics committee approval and all patients gave written informed consent.

(A) Cross-sectional observational study

This study enrolled 321 patients, who were consecutive, unselected attenders in the clinic. There were 245 females and 76 males of mean age 60 years (range 23–87) and mean disease duration nine years (range 1–48). Treatments comprised disease modifying drugs in 234 (73%) patients (including 152 on methotrexate and 31 on sulfasalazine), biologics (infliximab and etanercept) in 10 (3%), oral steroids in 41 (13%), intramuscular steroid in 20 (6%) and non-steroidal anti-inflammatory drugs and analgesics in 222 (69%).

(B) Treatment change observational study

This study lasted six months and enrolled 56 consecutive patients who were changing treatment and remained on therapy for six months. There were 49 females and seven males of mean age 55 years (range 20–79) and mean disease duration eight years (range 1–40). Six patients were starting biologics (infliximab or etanercept), 33 were starting methotrexate and 17 were starting other DMARDs including combination therapies. Forty patients (71%) had previously received disease modifying drugs, none had received biologics, 43 (77%) were receiving oral steroids and 45 (80%) non-steroidal anti-inflammatory drugs and analgesics.

Measures

We measured HAQ, EuroQol, SF-36 (divided into mental component summary (MCS) scores and physical component summary (PCS) scores) and NHP on a single occasion in the

Abbreviations: HAQ, Health Assessment Questionnaire; MCS, mental component summary; NHP, Nottingham Health Profile; PCS, physical component summary; QALY, quality adjusted life year

cross-sectional observational study and on two occasions six months apart in the treatment change observational study. We also recorded the disease activity score for 28-joint counts (DAS28), and the non-HAQ components of the Core Data Set, comprising 28 swollen joint counts, 28 tender joint counts, patient global assessments (100 mm visual analogue scores), physician global assessments (100 mm visual analogue scores), pain (100 mm visual analogue scores) and erythrocyte sedimentation rate.

Analysis

Data were analysed using SPSS version 10 to evaluate mean values and ranges, distributions and correlations between measures. As EuroQol showed a non-Gaussian distribution, Spearman's correlations were used.

RESULTS

Cross-sectional study

There was a general relation between HAQ and EuroQol scores (fig 1A). Patients with high HAQ scores (poor function) had

Figure 1 Cross sectional study: (A) relation of HAQ and EuroQol, (B) distribution of HAQ and (C) distribution of EuroQol.

Figure 2 Treatment change study: (A) relation of changes in HAQ and EuroQol, (B) distribution of changes in HAQ and (C) distribution of changes in EuroQol.

low EuroQol scores (poor health status) and vice versa with a moderate Spearman rank correlation ($r = 0.76$). However, many patients with high HAQ scores (poor function) also had high EuroQol (good health status) scores; 93 patients (29%) had HAQ scores over 2.0 of whom 26 (28%) had EuroQol scores over 0.5.

There was also a major difference in distribution of the two variables where HAQ scores showed a Gaussian distribution skewed to the left with a preponderance of lower scores (fig 1B), while EuroQol scores showed a biphasic, non-Gaussian, distribution with two separate peaks (fig 1C).

Table 1 Mean (SD) values and Spearman's correlations for absolute levels of HAQ and EuroQol in the cross-sectional study and changes in levels of HAQ and EuroQol in the treatment change study

Variable	Cross sectional			Treatment change		
	Mean (SD)	Correlation with HAQ	Correlation with EuroQol	Mean (SD)	Correlation with HAQ	Correlation with EuroQol
HAQ	1.5 (0.8)	–	–0.76	–0.2 (0.6)	–	0.08
EuroQol	0.45 (0.33)	–0.76	–	0.25 (0.35)	0.08	–
NHP physical function	37 (24)	0.75	–0.68	–6.0 (20)	0.38	0.01
SF-36 MCS	44 (14)	–0.29	0.43	4.0 (16)	–0.17	0.36
SF-36 PCS	28 (11)	–0.69	0.69	4.0 (10)	–0.03	0.42
SF-36 physical function	35 (26)	–0.70	0.64	8.0 (25)	0.13	0.41
DAS	4.7 (1.6)	0.55	–0.59	–1.2 (1.5)	0.64	–0.45
Pain	47 (27)	0.56	–0.61	–18 (29)	0.50	–0.54
ESR	33 (27)	0.27	–0.31	–18 (31)	0.30	–0.19
Tender joint counts	7.5 (7.2)	0.45	–0.50	–3.1 (7.3)	0.47	–0.31
Swollen joint counts	4.8 (4.1)	0.36	–0.36	–2.7 (4.7)	0.20	–0.22
Patients global	50 (28)	0.54	–0.54	–23 (31)	0.41	–0.39

DAS, Disease Activity Score; ESR, Erythrocyte Sedimentation Rate; HAQ, Health Assessment Questionnaire; NHP, Nottingham Health Profile; MCS, mental component summary; PCS, physical component summary.

Treatment change study

Changes in the HAQ and EuroQol in response to treatment were entirely unrelated (Spearman rank correlation $r = 0.08$) at an individual patient level (fig 2A). In terms of distribution, change in HAQ scores showed a Gaussian distribution skewed (fig 2B) to the left (lower scores) while change in EuroQol scores continued to show a biphasic distribution (fig 2C).

There were also differences in correlations with changes in other disease activity assessments (table 1). Treatment changes in EuroQol were associated with changes in other health utility measures like SF-36 PCS ($r = 0.42$), and MCS ($r = 0.36$) but not with change in a functional measure, the NHP physical function domain ($r = 0.01$). Conversely, treatment changes in HAQ were associated with changes in NHP physical function domain ($r = 0.38$) but not change in SF-36 PCS ($r = -0.03$).

DISCUSSION

Our results show that different patient-based measures provide different information about the effect of rheumatoid arthritis on patients and are consequently not equivalent. Our study was not intended to show which is best; as they measure different things it is likely they provide complementary information. However, our results provide strong evidence to reject the use of transformation from HAQ to EuroQol in an attempt to calculate QALYs; such transformations are widely used to assess cost-effectiveness of treatments^{4–6,9} by regulatory bodies.¹⁰ Since these determine drug availability, this is no longer an academic issue but a real clinical concern.

One approach to the problem of non-equivalence between HAQ and health utility measures such as EuroQol is to routinely collect utility measures like the EuroQol. However, this would not entirely resolve the problem of calculating cost effectiveness because there are important reservations about the usefulness of such utility measures in rheumatoid arthritis.¹¹ An obvious concern is that utility and health status measures incorporate a wide range of illness experience across all aspects of physical, emotional and social well-being; these are not necessarily easily captured in a single number. Just as different conventional disease activity assessments—such as joint counts and pain scores—give complementary but different information, so may different health status measures. Generic measures like EuroQol describe a limited number of health states, which may be insufficient to reflect the range of impacts of rheumatoid arthritis on health.

Furthermore, evaluation of utility measures in rheumatoid arthritis^{12–13} shows that direct measures, such as the “time trade

off” and “standard gamble” approaches, correlate poorly with indirect measures, such as EuroQol and SF-36. Direct utility measures involve complex choices. For example, the time trade off involves asking patients to choose between remaining in a state of ill health for a period of time or being restored to perfect health but having a shorter life expectancy. In the standard gamble, a patient is asked to choose between the certainty of surviving for a fixed period in a particular state of ill health or gambling on an intervention which could result in survival for the same period without disability but, alternatively, could mean immediate death. Half of rheumatoid arthritis patients¹² could not distinguish between the paired choices, suggesting they were not meaningful to them. Overall, although indirect measures like EuroQol appear more relevant than direct measures in rheumatoid arthritis,^{12–13} they are not ideal.

EuroQol determines the weight associated with a particular health state by using a standard descriptive system based on the views of healthy people—often termed “societal preference weights”—which may be very different to those of patients who have adapted to life with a chronic disabling disease. EuroQol has other difficulties in rheumatoid arthritis. For example disability, pain and depression questions ask about mild or moderate problems but not both, which forces scale compression in the mid-ranges, and the severe value is so extremely abnormal that few patients endorse it.¹¹

In summary, because the HAQ and EuroQol are demonstrably not equivalent, it is unwise to base economic evaluations on transformation of the HAQ to EuroQol. Further research is needed to identify the most useful measures for health economic studies in rheumatoid arthritis; approaches using Markov models are likely to be particularly relevant. The best measure to assess the impact of rheumatoid arthritis on health utility, and consequently to measure QALYs, remains uncertain; this uncertainty has been noted by Marra and colleagues¹⁴ and is also indicated by the range of different approaches used to measure the cost effectiveness of biologics in rheumatoid arthritis.¹⁵ Given the importance of defining the benefits of high-cost treatments it seems regrettable that we do not currently have a clearly identified method of capturing their benefits; further work in larger datasets is needed to define the optimal variables to capture health states in rheumatoid arthritis for inclusion within health economic studies. Other conventional measures, such as the SF-36, may be more relevant in assessing the economic impacts of treatment.

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